PATENT SPECIFICATION

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762,700

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COMPLETE SPECIFICATION

Improvements in or relating to Encapsulation

We, ALGINATE INDUSTRIES LIMITED, a British Company, of Walter House, Bedford Street, Strand, London, W.C.2, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to encapsulation, that is to say the enclosing of discrete portions of a material, for example globules of a liquid, individually in capsules. The technique of encapsulation is widely employed in certain industries, for example the pharmaceutical industry where it is frequently desired to provide separate doses of a substance, usually liquid, in a readily handleable form and protected from contamination, the capsule walls in this case usually being of some edible material that is dissolved by the digestive juices.

It has previously been proposed to encapsulate materials by employing a solidifiable liquid encapsulating medium and allowing a discrete portion, for example a globule in the case of a liquid, of the material to be encapsulated to fall downward in association with a film of the encapsulating medium, in such manner that the medium closes around the material to form a continuous layer, and finally solidifying the liquid encapsulating medium.

It is, moreover, known that a suitable encapsulating medium is a solution of sodium alginate which after surrounding the material to be encapsulated is caused to gel by immersion in a solution of calcium chloride, the method being to allow the falling mass to plunge straight into a bath of the liquid gelling medium. A disadvantage of this technique hitherto has been a limitation of the range of capsule size that can be produced, and furthermore, the resulting capsules are not always very regular in shape when they encounter the gelling bath.

According to the present invention, a process of encapsulation comprises the steps of forming around a discrete portion of the material to be encapsulated a film of liquid encapsulating medium, and causing the embryo capsule so produced to pass through an intermediate layer of liquid, which is immiscible and non-reactive with the encapsulating medium, into a gelling liquid which acts on the of liquid, which is immiscible and non-reactive with the encapsulating medium, into a gelling liquid which acts on the film of liquid encapsulating medium to gell it.

The layer of intermediate liquid slows down movements of the embryo capsules and reduces the effects of gravity, so that the tendency of the embryo capsule to disrupt when falling on the gelling medium through air, is minimised and also the capsules have time for the encapsulating film to assume a uniform thickness and, in the case of a liquid filling, for the globule of internal liquid to become spherical.

When the material to be encapsulated is a liquid, it should be immiscible with the encapsulating medium, and the embryo capsules may be formed by causing the liquid to be encapsulated to issue, from a source of supply, through a nozzle within an annular supply nozzle for the encapsulating liquid.

In the form of the process hereinafter described, the liquid encapsulating medium is a solution of an aliginate and the gelling liquid is a solution of a substance which renders the alginate insoluble.

In one form of the process the intermediate liquid is lighter than the gelling liquid and than the embryo capsules and floats on the gelling liquid, the embryo

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capsules being allowed to fall through the intermediate liquid into the gelling liquid below.

In another form of the process the intermediate liquid is heavier than the gelling liquid and the embryo capsules and the latter are produced below the surface of the intermediate liquid and allowed to float upwardly therethrough into the gelling liquid, which floats above the intermediate liquid. This permits of the production of capsules of light materials such as cod liver oil which cannot readily be made to sink into the gelling liquid.

It is to be understood that the present invention is not limited to the encapsulation of liquids nor materials which have medicinal or pharmaceutical properties. In suitable cases gases or solids may be encapsulated by the process according to the present invention which is characterised by the embryo capsules floating slowly up or down through the intermediate liquid into the gelling liquid. The invention includes apparatus for carrying the process into effect.

The following is a description by way of example of certain specific ways of carrying the invention into effect, reference being made to the accompanying diagrammatic drawings, in which:—

Figure 1 is a vertical section through one form of apparatus;

Figure 2 is a detail to a larger scale of part of the apparatus shown in Figure 1;

Figures 3 to 6 inclusive show stages in the formation of an embryo capsule;

Figure 7 is a view similar to Figure 1 of an alternative form of apparatus; and

Figure 8 is a detail of Figure 7.

Referring to the apparatus shown in Figures 1 to 6, this comprises a deep tank 11 above which is a capsule forming nozzle 12, the internal construction of which is shown in Figure 2. The nozzle 12 comprises an outer tube 13 and an inner co-axial tube 14. The lower end of the tube 13 is slightly below the end of the tube 14 and it has an inturned lip 15, the inner edge of which defines, between itself and the edge of the inner tube, an annular gap 16, the width of which can be adjusted by raising and lowering the inner tube 14 relatively to the tube 13. To this end the tube 14 has a screw threaded connection with the tube 13, as shown at 17, and after adjustment it can be secured by a lock nut 18. Encapsulating liquid can be fed to the annular space between the tubes 13 and 14 through a feed pipe 19 opening into the side of the outer tube.

The material to be encapsulated is fed into a third co-axial inner tube 20 which stops short well above the lower edges of the tubes 13, 14 and is held in place by being secured to a cap 21 threaded over the projecting upper end of the tube 14 and tightened by a lock nut 22. The inner tube 20 is supplied with the material which is to be encapsulated, which is allowed to fall, a drop at a time, inside the tube 14.

The encapsulating medium, a solution of sodium alginate, is fed through the pipe 19 into the annular space between the tubes 13 and 14 and at the bottom of these tubes it is directed inwardly through the annular gap 16. It is sufficiently viscous to form a continuous film across the bottom of the tubes as shown in Figure 3 at 23. The thickness of this film, and hence that of the wall of the capsule to be produced, can be varied by raising or lowering the tube 14 relative to tube 13. It will be understood that sodium alginate solution may be a very viscous material even in solutions of a strength of only 2 or 3% alginate in water. Consequently a relatively thick skin 23 can be allowed to form, and after the encapsulating process is over, when the skin is dried it will become quite thin. The material to be encapsulated is allowed to fall a drop at a time frm the lower end of the tube 20 as indicated in Figure 3 at 24 and in Figure 4, after the drop has fallen at 25.

The tank 11 is filled in its lower part with a solution of calcium chloride 26, which should preferably be say a foot deep, and over this is a layer, possibly 8″ deep of less dense liquid 27. This liquid may consist of a mixture of petroleum ether and carbon tetrachloride floating on the surface of the calcium chloride bath 26. Such a mixture is non-miscible with the calcium chloride bath and with the sodium alginate encapsulating medium, and it is inert, that is to say it has no gelling action on the latter. The upper level of the carbon tetrachloride petroleum ether mixture at 28 is just below the bottom of the nozzle 12 and when the material to be encapsulated falls on to the film 23, it makes it bulge downwardly until it touches the encapsulating liquid as shown in Figure 4. Eventually, when sufficient of the liquid to be encapsulated has dropped, it forms a globule 29 (Figure 5) which is large enough to cause the skin 23 to neck-in behind it and finally for the embryo capsule 30 thus formed to break away as shown in Figure 6 and fall through the gelling medium 27. Just before the breakaway, the film of encapsulating medium joins up across the neck 31

(Figure 5) to form an unbroken film around the globule 29 as shown in Figure 6 and to reform a continuous film 23 across the bottom of the nozzle 12 in readiness for the operation to be repeated with further material dropping from the inner pipe 20.

Owing to the fact that the capsule is supported by partial immersion in the liquid 27 while it is being formed, much larger capsules can be successfully produced than if the nozzle 12 were further from the surface of the liquid below it and the capsules had to be formed entirely in air. Moreover, the reduced speed of fall through the liquid layer 27 lessens the disruptive effect which would exist if the capsule struck the liquid surface with initial energy and the time taken in falling through the liquid layer 27 slowly gives the capsule an opportunity of assuming a nearly spherical shape before it reaches the gelling medium 26. This it enters gently and is gelled without distortion.

The size of the capsule formed can be controlled by altering the liquid level 28 relative to the level of the nozzle 12.

Adjustment of the ratio of the densities of the capsule 30 and the calcium chloride gelling medium 26 can be effected by varying the density of the latter; normally, this will be less than that of the capsule. Adjustment of the density of the floating liquid layer 27 in relation to the capsule density, for example by altering the proportion of petroleum ether, a low density liquid, to carbon tetrachloride which has high density, will vary the amount of support given to the capsule by said liquid layer and the rate of fall through it.

When the density of the material 25 to be encapsulated varies appreciably from that of the encapsulating medium, there is a tendency for the globule 29 of material to be encapsulated to rise or sink within the capsule mass and thereby make the film of encapsulating medium thinner at the top and thicker at the bottom, or *vice versa*. This may be overcome by using a filler to adjust the densities until they are approximately the same. It may also be overcome by causing the capsule mass, after its initial immersion in the gelling medium 26, to roll during its further descent so that the top and bottom of it are continually changing places. This might be done for example by inclined shelves 31, 32 within the lower part of tank 11 down which the capsules roll.

With the method according to the invention, it has been found possible to produce satisfactory capsules of very good spherical form as large as $\frac{3}{4}$" in diameter, and there is no reason to suppose that this is the upper size limit. Moreover, capsules have been made in which the encapsulated medium forming the capsule wall is as little as 1% of the total substance of the capsule mass. A further advantage of the present method is that splashing of the gelling medium as the capsule mass enters it, which splashes may reach and cause premature gelling of parts of the film of encapsulating medium across the bottom of the forming tubes, is entirely obviated.

Although in the process described above the material to be encapsulated impinges on the film of encapsulating medium in drop form, as an alternative, it is possible to arrange for the material to be encapsulated to flow continuously onto the film of encapsulating medium. The manner of formation of the capsule mass consisting of a globule of the material to be encapsulated in association with a film of the encapsulating medium is as described above, but in this case the material to be encapsulated does not separate as a discrete globule until it is divided off by the closing up above it of the film of encapsulating medium just before the mass breaks away.

In some cases the material to be encapsulated may be a light material such as cod liver oil which is capable of rendering the embryo capsules lighter than the gelling medium 26 and it may be undesirable to have the capsules floating at the interlayer between 26 and 27 as would occur with the apparatus shown in Figures 1 and 2. For this purpose the apparatus shown in Figure 7 may be adopted. This comprises a tank 33 in the bottom of which is a layer of heavy inert liquid 34 which may consist of a mixture, as in the case of Figures 1 and 2 of carbon tetrachloride and petroleum ether but in such proportions that the liquid is heavier than the gelling liquid 135 which forms a supernatant layer above it. For this purpose the carbon tetrachloride content of the liquid 34 is increased as compared with the apparatus of Figures 1 and 2. In the bottom of the tank 33 is a nozzle 35 having a lateral inlet pipe 36 to which sodium alginate solution is admitted from a pump 37 in periodic doses. In the centre of the alginate feed pipe is an upwardly directed nozzle 137 for the supply of cod liver oil from an inlet pipe 38 supplied by a pump 39. As can be seen from the enlarged view of the nozzle 35 shown in Figure 8, the end of the nozzle 137 is drawn out to a fine point at 40, like a fountain pen filler.

The pumps 37, 39 are operated by cams 41, 42 through rocker arms 43, 44. The rocker arms are mounted on pivots 45, 46 which are carried on slidable bases 47, 48 and the position of which between the cams 41, 42 and the pump plungers 49, 50 can be adjusted, so as to vary the strokes of the pumps. The cams 41, 42 are shaped to afford a gradual pumping stroke with a quick return, and the cam 41 is set to give a slight lead over the cam 42. The effect is that sodium alginate solution is pumped upwards into the liquid 34 through the annular space between the pipes 35, 137, and after an upward bulge of such material has begun to form at the upper lip 40, cod liver oil to be encapsulated is injected into it by the inner nozzle 137. The delivery strokes of the pumps are arranged to be such that at each stroke they form and detach a capsule complete with its covering skin in the liquid 34. The capsule rises through the liquid 34 as shown at 51 into the gelling liquid 135 through which it rises gradually to the surface. Here the outer layer of the capsule is gelled and the capsules collect on the upper surface and can be removed.

The capsules continue to set after they have been removed from the liquid and it may be found advisable to cause them to roll about on a tray, the surface of which is wet with a 25% solution of calcium chloride.

After about 20 minutes the capsules can be taken off and washed to remove excess calcium chloride and then allowed to dry, which thins the skin down by evaporation of water therefrom, whereon the product is ready for packing. Alternatively the globules taken from the aforesaid tray can be treated with acid to convert the calcium alginate to alginate acid and plasticised with glycerine before drying. If desired, the dried-alginic acid capsule can be exposed to ammonia gas to convert it into ammonium alginate which is soluble in water but is an efficient containing medium for oils.

The following are examples of the use of the apparatus of Figures 7 and 8.

Example I

In this example the material which is to be encapsulated is cod liver oil; the film of encapsulating medium is sodium alginate solution of considerable viscosity, say about 2% sodium alginate. The gelling liquid 135 is a calcium chloride solution of density 1.01 and the intermediate liquid 34 consists of equal parts of carbon tetrachloride and petroleum ether, the latter having a boiling range of 60° to 80° Centigrade. The alginate solution may have a strength of 1.44% on a dry weight basis. The internal diameter of the outer feed tube 35 may be 9 mm., the result is that the production of capsules containing cod liver oil of about the dimensions usual for such capsules when intended for medical use, i.e. about $^5/_{16}$" external diameter.

Example II

This is carried out similarly to Example I but instead of the encapsulating medium consisting of a sodium alginate solution, is consists of a mixture of solutions of sodium alginate and gelatine. In order to keep the gelatine in the liquid state in the mixture, the whole mixture and also the carbon tetrachloride petroleum ether mixture and the gelling liquid floating therein are maintained at a suitable elevated temperature, say about 50° C. The calcium chloride gels only the sodium alginate constituent of the encapsulating mixture, but this is sufficient to enable the capsules to be lifted from the surface of the bath, and as they cool the gelatine solidifies. The capsules are shaken as before so as to ensure that their contents are centralised and, if desired, after they have cooled and set, the calcium alginate can be washed out chamically, leaving a pure gelatine capsule which will entirely dissolve in the human body.

What we claim is:—

1. A process of encapsulation comprising the steps of forming around a discrete portion of the material to be encapsuled a film of liquid encapsulating medium, and causing the embryo capsule so produced to pass through an intermediate layer of liquid, which is immiscible and non-reactive with the encapsulating medium, into a gelling liquid which acts on the film of liquid encapsulating medium to gell it.

2. A process as claimed according to Claim 1, wherein the material to be encapsulated is a liquid, immiscible with the encapsulating medium, and the embryo capsules are formed by causing the liquid to be encapsulated to issue, from a source of supply, through a nozzle within an annular supply nozzle for the encapsulating liquid.

3. A process as claimed in Claim 1 or 2, wherein the liquid encapsulating medium is a solution of an alginate and the gelling liquid is a solution of a substance which renders the alginate insoluble.

4. A process as claimed in Claim 1 or 2 or Claim 3, wherein the intermediate liquid is lighter than the gelling liquid and than the embryo capsules and floats on the gelling liquid, the embryo capsules

being allowed to fall through the the intermediate liquid into the gelling liquid below.

5. A process as claimed in Claim 1 or 2 or Claim 3, wherein the intermediate liquid is heavier than the gelling liquid and the embryo capsules and the latter are produced below the surface of the intermediate liquid and allowed to float upwardly therethrough into the gelling liquid, which floats above the intermediate liquid.

6. A process as claimed in any one of the preceding claims wherein, after the encapsulating film has been subjected to the action of the gelling liquid, the capsules are caused to roll over and over while still setting, to centralise the encapsulating material in the film.

7. Apparatus for the production of capsules substantially as described with reference to and shown in the accompanying drawings, Figures 1 to 6 or Figures 7 and 8.

8. A process for the production of capsules substantially as described with reference to Figures 1 to 6 or to Figures 7 and 8 hereof.

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PROVISIONAL SPECIFICATION
No. 14465 A.D. 1954

Improvements in or relating to Encapsulation

We, ALGINATE INDUSTRIES LIMITED, a British Company, of Walter House, Bedford Street, Strand, London, W.C.2, do hereby declare this invention to be described in the following statement:—

This invention relates to encapsulation, that is to say the enclosing of discrete portions of a material for example globules of a liquid, individually in capsules. The technique of encapsulation is widely employed in certain industries, for example the pharmaceutical industry where it is frequently desired to provide separate doses of a substance, usually liquid, in a readily handleable form and protected from contamination, the capsule walls in this case usually being of some edible material that is dissolved by the digestive juices.

It has previously been proposed to encapsulate materials by employing a solidifiable liquid encapsulating medium and allowing a discrete portion, for example a globule in the case of a liquid, of the material to be encapsulated to fall downward in association with a film of the encapsulating medium, in such manner that the medium closes around the material to form a continuous layer, and finally solidifying the liquid encapsulating medium.

It is, moreover, known that a suitable encapsulating medium is a solution of sodium alginate which after surrounding the material to be encapsulated is caused to gel by immersion in a solution of calcium chloride, the method being to allow the falling mass to plunge straight into a bath of the liquid gelling medium. A disadvantage of this technique hitherto has been a limitation of the range of capsule size that can be produced, and furthermore, the resulting capsules are not always very regular in shape when they encounter the gelling bath.

According to the present invention, instead of falling through air straight into the gelling medium, the mass of encapsulating medium surrounding material to be encapsulated passes first through a layer of a liquid which is of less density than the gelling medium so that it floats on top of it, is non-miscible with the encapsulating medium and the gelling medium and has no gelling effect on the encapsulating medium.

The layer of liquid above the gelling medium serves to support the falling capsule mass to some extent and to slow down its rate of fall as compared with the rate of fall in air; it thereby reduces the tendency of the mass to disrupt and also affords an opportunity for the capsule to attain a more nearly spherical shape before encountering the gelling medium.

Preferably, the delivery apparatus from which the capsule mass starts its fall is situated close above the surface of the liquid layer floating on the gelling medium, so that the capsule is actually partially supported by immersion in said liquid while it is in the process of formation. This enables considerably larger capsules that has hitherto been possible by this method to be produced.

In one method of carrying the invention into effect, described by way of example, the apparatus comprises inner and outer coaxial tubes mounted vertically over a bath of calcium chloride gelling medium. The lower end of the outer tube is slightly below that of the inner tube, and it has an inturned lip the inner edge of which defines between itself and the edge of the inner tube an annular gap, the width of which can be adjusted by raising

and lowering the inner tube with respect to the outer.

The encapsulating medium, a solution of sodium alginate, is fed into the space between the inner and outer tubes, and passes inwardly through the annular gap at the lower ends of the tubes. It is sufficiently viscous to form a continuous film across the bottom of the tubes; the thickness of this film, and hence that of the wall of the capsule to be produced, can be varied by the aforementioned relative adjustment of the tubes. The material to be encapsulated, in this case a liquid, is fed into a third coaxial tube of smaller diameter than the other tubes, which third tube stops short well above the lower edges of the outer tubes and is arranged to permit the material to fall a drop at a time towards the film of encapsulating medium. Both the annular space containing the encapsulating medium and the small diameter tube are fed continuously with encapsulating medium and material to be encapsulated respectively.

As a succession of drops of material to be encapsulated fall from the small diameter tube and impinge on the film of encapsulating medium, the film bulges downwardly to an increasing extent and then necks in behind the globule of material to be encapsulated, finally breaking away to allow the whole mass to fall toward the gelling medium. Just before the breakaway, the encapsulating medium joins up across the upper surface of the globule of material to be encapsulated to form an unbroken film around it, while the continuous film across the bottom of the tubes reforms in readiness for the next drop of material to be encapsulated.

In accordance with the invention, a layer of less dense liquid, comprising in this example a mixture of petroleum ether and carbon tetrachloride, is provided floating on the surface of the calcium chloride gelling medium. This mixture is non-miscible with the gelling medium and the sodium alginate encapsulating medium, and it has no gelling action on the latter. The capsule mass, therefore, falls through it unchanged.

The bottoms of the tubes on which the capsule mass is formed are situated close above the upper surface of the floating layer of liquid, and in this way the capsule is supported by partial immersion while it is actually being formed, which enables much larger capsules to be successfully produced. Moreover, the reduced speed of fall through said liquid layer lessens the disruptive effect on the capsule and also gives it an opportunity of attaining a more nearly spherical shape before reaching the gelling medium. The size the capsule formed is dependent upon the extent to which the capsule is immersed during formation, so that this can be controlled by raising or lowering the forming tubes with respect to the floating liquid layer.

Adjustment of the ratio of the densities of the capsule and the calcium chloride gelling medium can be effected by varying the density of the latter; normally, this will be less than that of the capsule. Adjustment of the density of the floating liquid layer in relation to the capsule density, for example by altering the proportion of petroleum ether, a low density liquid, to carbon tetrachloride which has high density, will vary the amount of support given to the capsule by said liquid layer and the rate of fall through it.

When the density of the material to be encapsulated varies appreciably from that of the encapsulating medium, there is a tendency for the globule of material to be encapsulated to rise or sink within the capsule mass and thereby make the film of encapsulating medium thinner at the top and thicker at the bottom, or *vice versa*. This may be overcome by using a filler to adjust the densities until they are approximately the same. It may also be overcome by causing the capsule mass, after its initial immersion in the gelling medium, to roll during its further descent so that the top and bottom of it are continually changing places.

As has already been mentioned, the process described is a continuous flow process in which the feed to the forming tubes of encapsulating medium and material to be encapsulated is constant. It has also been proposed hitherto to operate an intermittent flow process in which a charge of an encapsulating medium and a charge of material to be encapsulated are fed to the forming tubes periodically, but this involves the disadvantage that special pumps and driving mechanism therefore are required which makes the whole apparatus more complicated and costly. With the method and apparatus described, large numbers of capsules can be produced at a rapid rate by having a plurality of forming tube assemblies mounted over a common gelling bath.

With the method according to the invention, it has been found possible to produce satisfactory capsules of very good spherical form as large as $\frac{3}{4}$" in diameter, and there is no reason to suppose that this is the upper size limit. Moreover, capsules have been made in which the encapsulated medium forming the capsule wall is as little as 1% of the total substance of the capsule mass. A further advantage of

the present method is that splashing of the gelling medium as the capsule mass enters it, which splashes may reach and cause premature gelling of parts of the film of encapsulating medium across the bottom of the forming tubes, is entirely obviated.

Although in the process described above the material to be encapsulated impinges on the film of encapsulating medium in drop form, as an alternative, it is possible to arrange for the material to be encapsulated to flow continuously on to the film of encapsulating medium. The manner of formation of the capsule mass consisting of a globule of the material to be encapsulated in association with a film of the encapsulating medium is as described above, but in this case the material to be encapsulated does not separate as a discrete globule until it is divided off by the closing up above it of the film of encapsulating medium just before the mass breaks away.

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PROVISIONAL SPECIFICATION
No. 21190 A.D. 1954

Improvements in or relating to Encapsulation

We, ALGINATE INDUSTRIES LIMITED, a British Company, of Walter House, Bedford Street, Strand, London, W.C.2, do hereby declare this invention to be described in the following statement:—

This invention comprises improvements in or relating to encapsulation.

The invention is cognate with that described in Patent Application No. 14465/54, according to which capsules of materials such as, for example, cod liver oil or medicaments or other substances are formed by allowing a discrete portion of the material to be encapsuled to pass through an intermediate liquid in association with a film of the encapsulating medium in such manner that the medium closes around the material to form a continuous layer and then passes into a body of gelling liquid where the encapsulating film is gelled.

In the aforesaid patent application the intermediate liquid floats on top of the gelling liquid and the material with its encapsulating layer falls through the liquids. The material to be encapsulated is allowed to fall through a tube by gravity on to a film of the encapsulating medium which is stretched below it between the edges of an annular delivery orifice which surrounds the lower end of the tube of material to be encapsulated, and which envelops this material before passing through the intermediate liquid into the gelling liquid.

It has now been found that it is possible to invert the procedure, that is to say, the material to be encapsulated can be injected upwards into a globule of encapsulating medium which is maintained in the lower part of a surrounding intermediate liquid through which the embryo capsules can float upwards and on the surface of which the gelling solution will float. This permits of the production of capsules of light materials such as cod liver oil which cannot readily be made to sink into the gelling liquid.

It is to be understood that the present invention is not limited to the encapsulation of liquids nor materials which have medicinal or pharmaceutical properties. In suitable cases gases or solids may be encapsuled by the process acording to the present invention which is characterised by the capsules floating upwards through a liquid into a super-incumbent layer of a gelling liquid.

The following is a description by way of example of particular methods by which the invention may be carried into effect:—

EXAMPLE I.

In this example the material which is to be encapsulated is cod liver oil; the film of encapsulating medium in which the oil is to be enclosed is an alginate solution of suitable viscosity; the gelling liquid is a calcium chloride solution and the intermediate liquid upon which the gelling liquid floats consists of a mixture of carbon tetrachloride and petroleum ether. Mixtures of carbon tetrachloride and petroleum ether can be made over a wide range of proportions which afford a corresponding range of specific gravities adjustable to give parctically any density, and hence size of capsule required. If the density is adjusted so as to differ only slightly from the embryo capsules of cod liver oil encased in a layer of alginate solution, these capsules will rise slowly through the mixture of carbon tetrachloride and petroleum ether so that they have ample time to assume a spherical shape before they enter the gelling liquid. In the present case a feed pipe 9 mm. internal diameter is arranged so that it stands mouth upward in a bath consisting of equal parts of carbon tetrachloride and petroleum ether, the latter having a boiling range

of 60 to 80° C. On top of the tetrachloride and petroleum ether bath, is a layer of calcium chloride solution of density 1.01. An alginate solution of a strength of 1.44% on a dry weight basis is supplied to the 9 mm. fed pipe. The alginate employed is such as to have a viscosity of 800 centistokes when made up in a 1% solution at 25° C.

In the centre of the alginate feed pipe is an upwardly directed glass nozzle for the supply of cod liver oil. The glass nozzle is drawn out to a fine point like a fountain pen filler. Means are provided for the continuous supply of an alginate sclution at such a rate that globules tend to form in the tetrachloride and petroleum ether mixture at the top of the feed pipe and periodically to detach themselves and float upwards into the calcium chloride solution. A positive piston feed is provided for the cod liver oil such as to eject through the nozzle periodic single doses of oil. Each dose as it comes out of the nozzle finds itself surrounded with a layer of alginate solution and if the rates of feed of the alginate solution and the cod liver oil are correct, a globule of alginate solution containing the cod liver oil will detach itself from the top of the feed pipe and rise slowly into the gelling liquid above. In rising the globule has time to assume a truly spherical form. The gelling solution solidifies the external surface of the alginate solution and the globules collect on the surface of the calcium chloride.

From here the globules are lifted and laid upon a horizontal tray, the surface of which is wet with a 25% solution of calcium chloride. The tray is mounted so that it executes a rapid circular movement in a horizontal plane which causes the globules to turn over and over while their inner part behind the outer skin gels. The effect of this is to ensure that the cod liver oil globule enclosed in the capsule is properly centred, so that the skin around it is of even thickness. This shaking process, with a view to centralising the contents wiithin the capsule, is a further important feature of the present invention. After about twenty minutes the capsules can be taken off and washed to remove excess calcium chloride and then allowed to dry, which thins the skin down by evaporation of water therefrom, whereon the product is ready for packing. Alternatively the globules taken from the vibrating tray can be treated with acid to convert the calcium alginate to alginic acid and plasticised with glycerine before drying. If desired, the dry-alginic acid capsule can be exposed to ammonia gas to convert it into ammonium alginate which is soluble in water but is an efficient containing medium for oils.

EXAMPLE II

This is carried out similarly to Example I but instead of the encapsulating medium consisting of a sodium alginate solution, it consists of a mixture of solutions of sodium alginate and gelatine. In order to keep the gelatine in the liquid state in the mixture, the whole mixture and also the carbon tetrachloride petroleum ether mixture and the gelling liquid floating thereon are maintained at a suitable elevated temperature, say about 50° C. The calcium chloride gels only the sodium alginate constituent of the encapsulating mixture, but this is sufficient to enable the capsules to be lifted from the surface of the bath, and as they cool the gelatine solidifies. The capsules are shaken as before so as to ensure that their contents are centralised and, if desired, after they have cooled and set, the calcium alginate can be washed out chemically, leaving a pure gelatine capsule which will entirely dissolve in the human body.

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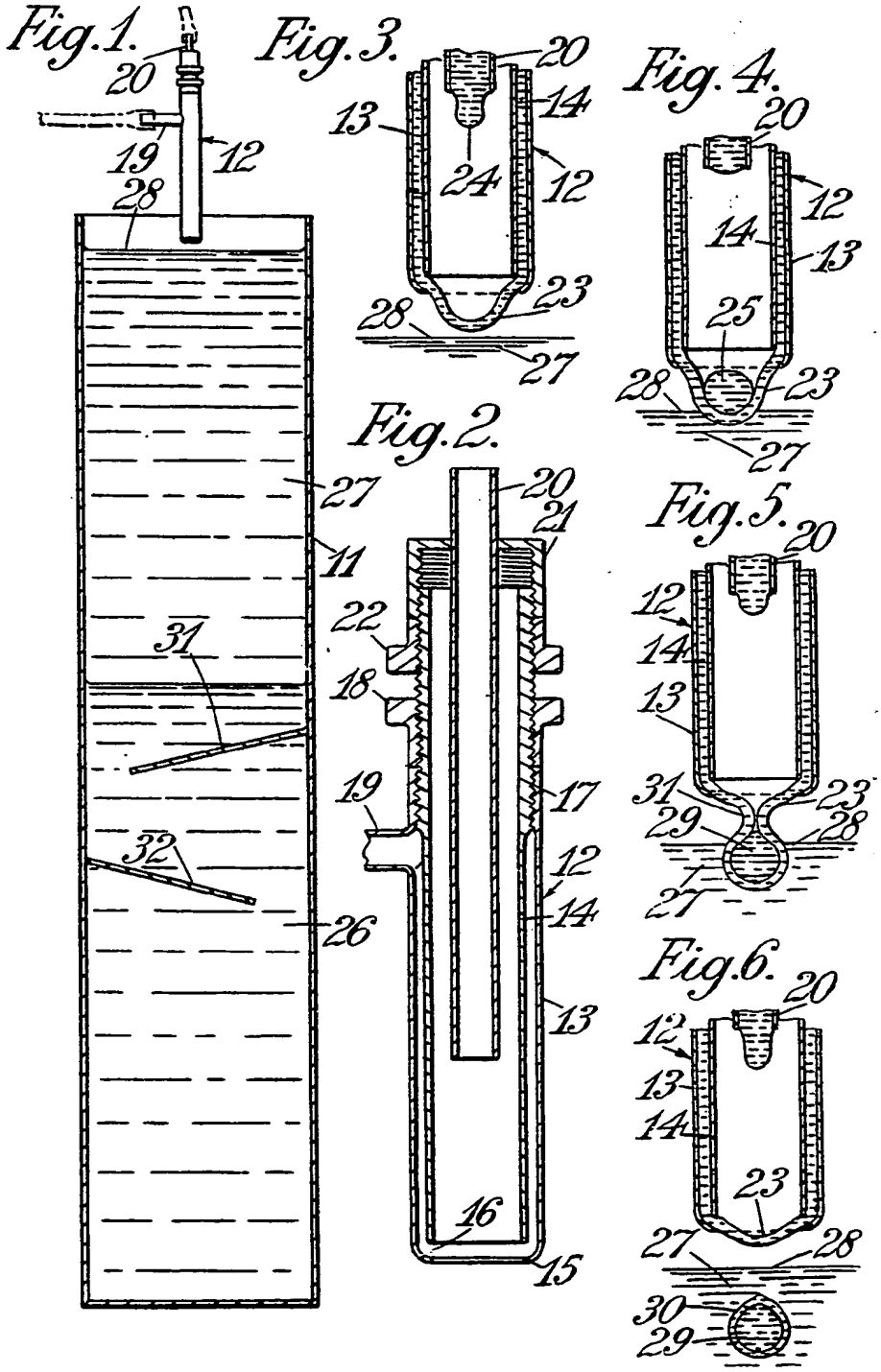

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Fig. 4.

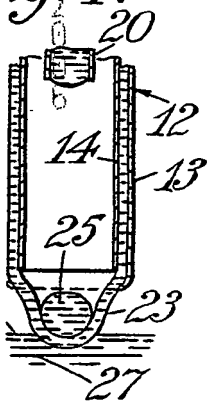


Fig. 5.

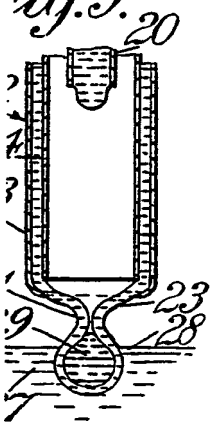
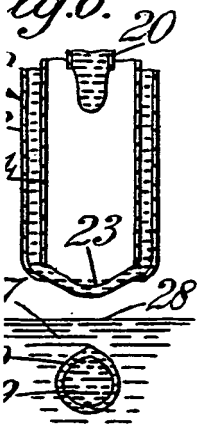


Fig. 6.



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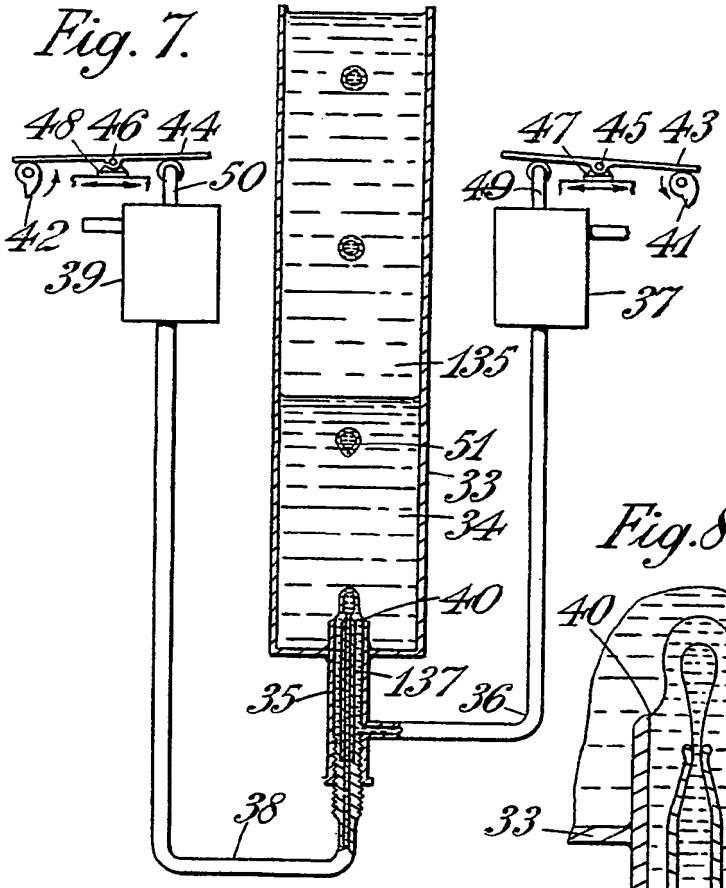
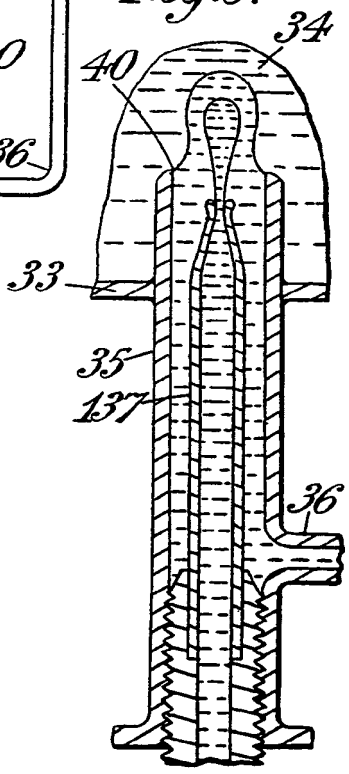


Fig. 8.



762700 COMPLETE SPECIFICATION
2 SHEETS This drawing is a reproduction of the Original on a reduced scale
Sheets 1 & 2

Fig.1.

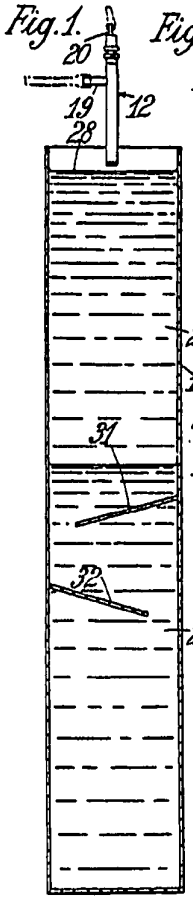


Fig.3.

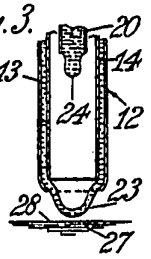


Fig.2.

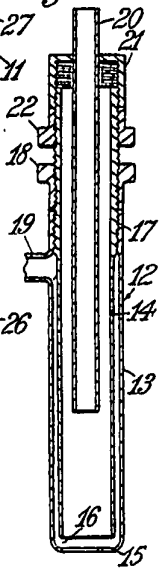


Fig.4.

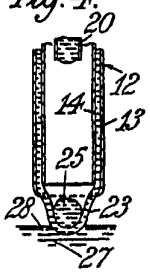
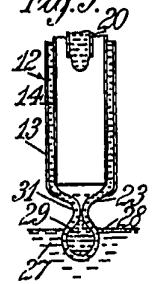


Fig.5.



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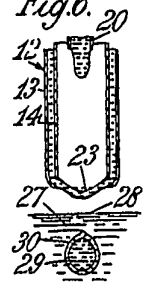

Fig.7.

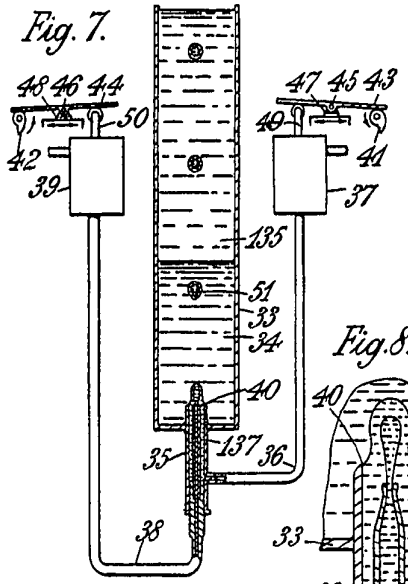

Fig.8.